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<u>Set</u> <u>Name</u>	<u>Query</u>	<u>Hit</u> <u>Count</u>	<u>Set</u> <u>Name</u> result set
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
L15	L14 and (ciclesonide)	1	L15
L14	L13 and @ad<20020405	135	L14
L13	L12 and l11	294	L13
L12	(((\$steroid\$3) same (solution or dissol\$8))	14575	L12
L11	((betamimetic or (beta near4 agonist) or formoterol or salbutamol or albuterol or "TA 2005") same (suspension or dispersion or particl\$3 or particulate or powder))	1477	L11
	DB=PGPB,USPT; PLUR=YES; OP=OR		
L10	((betamimetic or (beta near4 agonist) or formoterol or salbutamol or albuterol or "TA 2005") same (suspension or dispersion or particl\$3 or particulate or powder))	1293	L10
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI,TDBD; PLUR=YES; OP=OR		
L9	L8 NOT L5	2	L9
L8	L7 and L6	6	L8
L7	(ciclesonide same (solution or dissol\$8))	41	L7
L6	(formoterol same (suspension or dispersion or particl\$3 or particulate or powder))	515	L6
	DB=PGPB,USPT; PLUR=YES; OP=OR		
L5	L4 and (ciclesonide same (solution or dissol\$8))	4	L5
L4	L3 and (formoterol same (suspension or dispersion or particl\$3 or particulate or	187	L4

powder))

L3 (424/45 or 424/46).ccls.3023 L3L2 (Philip near Jinks) AND @pd>200612020 L2L1 (Martin near Oliver) AND @pd>200612021 L1

END OF SEARCH HISTORY

(FILE 'HOME' ENTERED AT 21:13:59 ON 11 AUG 2007)

FILE 'CAPLUS, MEDLINE, USPATFULL, BIOSIS, EMBASE' ENTERED AT 21:14:54 ON  
11 AUG 2007

L1 4005 S ((BETAMIMETIC OR (BETA (4A) AGONIST) OR FORMOTEROL OR SALBUTA  
L2 18653 S ((CORTICOSTEROID OR STEROID?) (P) (SOLUTION OR DISSOL?))  
L3 116 S L1 AND L2  
L4 116 S L1 (S) L2  
L5 22 S L4 NOT PD>20020405  
L6 17 DUPLICATE REMOVE L5 (5 DUPLICATES REMOVED)  
L7 17 FOCUS L6 1-

=> d que L1

L1 4005 SEA ((BETAMIMETIC OR (BETA (4A) AGONIST) OR FORMOTEROL OR  
SALBUTAMOL OR ALBUTEROL OR (TA(W) 2005)) (P) (SUSPENSION OR  
DISPERSION OR PARTICL? OR PARTICULATE OR POWDER))

=> d que L2

L2 18653 SEA ((CORTICOSTEROID OR STEROID?) (P) (SOLUTION OR DISSOL?))

L7 ANSWER 6 OF 17 MEDLINE on STN

TI Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature.

AB BACKGROUND: Asthma and chronic obstructive pulmonary disease (COPD) are common diseases of the airways and lungs that have a major impact on the health of the population. The mainstay of treatment is by inhalation of medication to the site of the disease process. This can be achieved by a number of different device types, which have wide variations in costs to the health service. A number of different inhalation devices are available. The pressurised metered-dose inhaler (pMDI) is the most commonly used and cheapest device, which may also be used in conjunction with a spacer device. Newer chlorofluorocarbons (CFC)-free inhaler devices using hydrofluoroalkanes (HFAs) have also been developed. The drug is dissolved or suspended in the propellant under pressure. When activated, a valve system releases a metered volume of drug and propellant. Other devices include breath-actuated pMDIs (BA-pMDI), such as Autohaler and Easi-Breathe. They incorporate a mechanism activated during inhalation that triggers the metered-dose inhaler. Dry powder inhalers (DPI), such as Turbohaler, Diskhaler, Accuhaler and Rotahaler, are activated by inspiration by the patient. The powdered drug is dispersed into particles by the inspiration. With nebulisers oxygen, compressed air, or ultrasonic power is used to break up solutions or suspensions of medication into droplets for inhalation. The aerosol is administered by mask or by a mouthpiece. There has been no previous systematic review of the evidence of clinical effectiveness and cost-effectiveness of these different inhaler devices. OBJECTIVES: To review systematically the clinical effectiveness and cost-effectiveness of inhaler devices in asthma and COPD. METHODS: The different aspects of inhaler devices were separated into the most clinically relevant comparisons. Methods involved systematic searching of electronic databases and bibliographies for randomised controlled trials (RCTs) and systematic reviews. Pharmaceutical companies and experts in the field were contacted for further information. Trials that met the inclusion criteria were appraised and data extraction was under-taken by one reviewer and checked by a second reviewer, with any discrepancies being resolved through agreement. RESULTS--IN VITRO CHARACTERISTICS VERSUS IN VIVO TESTING AND CLINICAL RESPONSE: There is evidence that when comparative testing is performed on inhaler devices using the same methods, there is some correlation between particle size measurements and clinical response. However, the measurements are dependent upon the methods used, and a single measure of a device in isolation is of limited value. Also, there is little data on comparing devices of different types. There is currently insufficient data to verify the ability of in vitro assessments to predict inhaler performance in vivo. RESULTS--EFFECTIVENESS OF METERED-DOSE INHALERS FOR THE DELIVERY OF CORTICOSTEROIDS IN ASTHMA: The review of three trials in children and 21 trials in adults demonstrated no evidence to suggest clinical benefits of any other inhaler device over a pMDI in corticosteroid delivery. RESULTS--EFFECTIVENESS OF METERED-DOSE INHALERS FOR THE DELIVERY OF BETA-AGONISTS IN STABLE ASTHMA: In children, 11 studies were reviewed, of which seven compared the Turbohaler with the pMDI. One study found a significant treatment difference in peak expiratory flow rate, although there were differences in the patients' baseline characteristics. In adults, a review of 70 studies found no demonstrable difference in the clinical bronchodilator effect of short-acting b2-agonists delivered by the standard pMDI compared with that produced by any other DPI, HFA-pMDI or the Autohaler device. The finding that HFA-pMDIs may reduce treatment failure and oral steroid requirement in beta-agonist delivery needs further confirmatory research in adequately randomised clinical trials. RESULTS--EFFECTIVENESS OF NEBULISERS VERSUS METERED-DOSE INHALERS FOR THE DELIVERY OF BRONCHODILATORS IN STABLE ASTHMA: In children, three included trials compared different devices with a nebuliser and demonstrated no evidence of clinical superiority of

nebulisers over inhaler devices in bronchodilator delivery. A total of 23 studies in adults found no equivalence for the main pulmonary outcomes and no evidence of difference in other outcomes. RESULTS--EFFECTIVENESS OF METERED-DOSE INHALERS FOR THE DELIVERY OF BETA-AGONISTS IN COPD: Only two studies were included in this review. No evidence of clinical difference was found in beta-agonist delivery. RESULTS--EFFECTIVENESS OF NEBULISERS VERSUS METERED-DOSE INHALERS FOR THE DELIVERY OF BRONCHODILATORS IN COPD: Evidence from 14 trials demonstrated equivalence for the main outcomes of pulmonary function. For other outcomes there was no evidence of treatment difference in bronchodilator delivery. RESULTS--PATIENTS' ABILITY TO USE METERED-DOSE INHALERS: Differences among studies and the heterogeneity of the results make it difficult to draw conclusions about inhaler technique differences between device types. The review of technique after teaching the correct technique suggests that there is no difference in patients' ability to use DPI or pMDIs. RESULTS--ECONOMIC ANALYSIS: The total number of NHS prescriptions for inhaler therapy for asthma in 1998 was over 31 million, with a net ingredient cost in excess of 392 million GB pounds. This economic assessment uses decision analysis to estimate the relative cost-effectiveness of inhaler devices for the delivery of bronchodilator and corticosteroid inhaled therapy. Overall, there were no differences in patient outcomes among the devices. On the assumption that the devices were clinically equivalent, pMDIs were the most cost-effective devices for asthma treatment. CONCLUSIONS: This systematic review examined the evidence from clinical trials evaluating the clinical effectiveness of different inhaler devices in the delivery of inhaled corticosteroids and beta2-bronchodilators for patients with asthma and COPD. The evidence from the published clinical literature demonstrates no difference in clinical effectiveness between nebulisers and alternative inhaler devices compared to standard pMDI with or without a spacer device. The cost-effectiveness evidence therefore favours pMDIs (or the cheapest inhaler device) as first-line treatment in all patients with stable asthma unless other specific reasons are identified. Patients can use pMDIs as effectively as other inhaler devices as long as the correct inhalation technique is taught. CONCLUSIONS--RECOMMENDATIONS FOR RESEARCH: Further clinical trials are required to demonstrate any differences in the clinical effectiveness and cost-effectiveness of inhaler devices and nebulisers compared with pMDIs. These should be of sufficient statistical power and methodological rigour to demonstrate any clinical benefit. Trials should be undertaken in community settings to ensure the generalisability of results. Outcome measures should be more patient-centred and report adverse effects more completely. Reporting of data from trials should be improved.

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DOCUMENT NUMBER: PubMed ID: 11701099  
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AUTHOR: Brocklebank D; Ram F; Wright J; Barry P; Cates C; Davies L; Douglas G; Muers M; Smith D; White J  
CORPORATE SOURCE: Department of Epidemiology and Public Health, Bradford Hospitals NHS Trust, UK.  
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L7 ANSWER 1 OF 17 MEDLINE on STN

TI Treatment of acute severe asthma with inhaled albuterol delivered via jet nebulizer, metered dose inhaler with spacer, or dry powder.

AB Despite the increasing use of dry powder formulations in the ambulatory setting, there is a paucity of information on the efficacy of this therapeutic modality to treat acute severe asthma. In addition, studies that compared wet nebulization vs metered dose inhalers formulated with chlorofluorocarbon (CFCMDI) attached to holding chambers have yielded discrepant results. Thus, it is unclear which of the three delivery systems would elicit a superior bronchodilator response, particularly in patients with life-threatening asthma. In a prospective, randomized open design, we studied the response to inhaled albuterol (salbutamol) in 27 adult asthmatics presenting to the emergency department (ED) with an FEV1 <30% predicted. Subjects were treated with one of the following regimens (nine subjects in each group): group A, mean (SD) baseline FEV1 of 0.7 (0.2) L, received albuterol solution, 5 mg, via a nebulizer (Puritan-Bennett Raindrop; Lawrenceville, Ga) impelled with oxygen (O2) at 8 L/min; group B, baseline FEV1 of 0.6 (0.15) L, received albuterol, 400 microg, via a CFCMDI attached to a 145-mL valved aerosol holding chamber (Aerochamber; Trudell Medical; London, ON); and group C, baseline FEV1 of 0.6 (0.17) L, received albuterol powder, 400 microg, by another means (Rotahaler; Glaxo; Research Triangle Park, NC). All groups received the respective treatments on arrival in the ED, every 30 min during the first 2 h, and then hourly until the sixth hour. Clinical parameters and FEV1 were recorded on ED admission and 15 min after each dose of albuterol. At the time of ED admission, all patients also received continuous O2 and one dose of I.V. steroids (dexamethasone, 8 mg). The total dose of inhaled albuterol administered during the 6-h treatment was 45 mg of nebulized solution in group A and 3,600 microg of albuterol aerosol and dry powder in groups B and C, respectively. No significant differences were found in the population demographics, baseline FEV1, and arterial blood gas values on air. FEV1 improved significantly in all patients after the 6 h of treatment. The 6-h area under the curve FEV1 improved similarly with the three delivery methods despite differences in the total dose administered. No patient was discontinued during the trial or admitted to hospital and no evidence of cardiovascular adverse events was apparent in any of the study groups. These data support the view that the three delivery methods appear adequate to treat subjects with acute severe asthma.

L7 ANSWER 2 OF 17 USPATFULL on STN

TI Novel liposome composition for the treatment of interstitial lung diseases

AB A non-conventional lipid particle formulation for the sustained release and delivery of steroids into deep lung is disclosed. The formulation provides prolonged release of the drug, improved therapeutic ratio, lower toxicity, reduced systemic side effects, and stability for several months. The formulation is in particular suitable for treatment of interstitial lung diseases.

L7 ANSWER 3 OF 17 USPATFULL on STN

TI Stabilized preparations for use in metered dose inhalers

AB Stabilized dispersions are provided for the delivery of a bioactive agent to the respiratory tract of a patient. The dispersions preferably comprise a plurality of perforated microstructures dispersed in a suspension medium that typically comprises a hydrofluoroalkane propellant. As density variations between the suspended particles and suspension medium are minimized and attractive forces between microstructures are attenuated, the disclosed dispersions are particularly resistant to degradation, such as, by settling or

flocculation. In particularly preferred embodiments, the stabilized dispersions may be administered to the lung of a patient using a metered dose inhaler.

- L7 ANSWER 4 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Antiasthmatic pharmaceutical composition containing formoterol and rofleponide or their salts and derivatives  
AB A composition or kit having as a first active ingredient formoterol (I), or a salt or solvate derivative thereof, and having as a second active ingredient rofleponide (II), or a fatty acid ester thereof is disclosed. Also disclosed are methods for treating respiratory disorders using this composition or kit. II palmitate 10, dipalmitoylphosphatidylcholine 63, dimyristoylphosphatidylcholine 24, sodium dipalmitoylphosphatidylglycerol 3, and racemic  $\alpha$ -tocopherol 0.1 parts were dissolved in 1300 parts tertiary butanol and the soln. was freeze-dried to obtain a powder which was micronized to particle size of less than 5 $\mu$ m. I fumarate dihydrate 0.5 parts was mixed with 79.5 parts of lactose monohydrate and micronized. This micronized mixture (80 parts) was added to the steroid/lipid freeze-dried powder (20 parts) and filled into a capsule for use in a dry powder inhaler.
- L7 ANSWER 5 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
TI Enhanced drug delivery through reformulating MDIs with HFA propellants-drug deposition and its effect on preclinical and clinical programs  
AB The use of CFCs in metered dose inhalers (MDIs) will be discontinued in the very near future. Thus far, one non-CFC product, Airomir (HFA, salbutamol), an HFA-134a based salbutamol sulfate formulation has been approved and introduced in fifteen countries. The development program entailed inventing new formulation and container/closure technol. to accommodate the different chemical and phys. properties of HFA-134a. Results of the preclin. program showed that HFA did not alter the known safety profile of salbutamol. An extensive clin. program demonstrated safety and efficacy of HFA salbutamol, and showed remarkable similarity to existing CFC salbutamol products. The next product under development is HFA-beclomethasone (HFA-BDP). There was significant need and opportunity to improve delivery characteristics of steroids in order to reduce unwanted oropharynx deposition, and increase large and small airway lung deposition. This was accomplished by creating a soln. aerosol with a particle size of 1.1  $\mu$ . Results of clin. scintigraphy studies using technetium-99m radiolabeled aerosols in asthmatics showed that 56% of the drug was deposited in the lungs with concomitant decreased oropharynx deposition compared with typical CFC-BDP lung deposition of 5-30%. Clin. studies are well underway, the results of which have thus far demonstrated safety and efficacy.
- L7 ANSWER 6 OF 17 MEDLINE on STN  
TI Comparison of the effectiveness of inhaler devices in asthma and chronic obstructive airways disease: a systematic review of the literature.  
AB BACKGROUND: Asthma and chronic obstructive pulmonary disease (COPD) are common diseases of the airways and lungs that have a major impact on the health of the population. The mainstay of treatment is by inhalation of medication to the site of the disease process. This can be achieved by a number of different device types, which have wide variations in costs to the health service. A number of different inhalation devices are available. The pressurised metered-dose inhaler (pMDI) is the most commonly used and cheapest device, which may also be used in conjunction with a spacer device. Newer chlorofluorocarbons (CFC)-free inhaler devices using hydrofluoroalkanes (HFAs) have also been developed. The drug is dissolved or suspended in the propellant under pressure. When activated, a valve system releases a metered volume of drug and propellant. Other devices include breath-actuated pMDIs (BA-pMDI), such

as Autohaler and Easi-Breathe. They incorporate a mechanism activated during inhalation that triggers the metered-dose inhaler. Dry powder inhalers (DPI), such as Turbohaler, Diskhaler, Accuhaler and Rotahaler, are activated by inspiration by the patient. The powdered drug is dispersed into particles by the inspiration. With nebulisers oxygen, compressed air, or ultrasonic power is used to break up solutions or suspensions of medication into droplets for inhalation. The aerosol is administered by mask or by a mouthpiece. There has been no previous systematic review of the evidence of clinical effectiveness and cost-effectiveness of these different inhaler devices. OBJECTIVES: To review systematically the clinical effectiveness and cost-effectiveness of inhaler devices in asthma and COPD. METHODS: The different aspects of inhaler devices were separated into the most clinically relevant comparisons. Methods involved systematic searching of electronic databases and bibliographies for randomised controlled trials (RCTs) and systematic reviews. Pharmaceutical companies and experts in the field were contacted for further information. Trials that met the inclusion criteria were appraised and data extraction was under-taken by one reviewer and checked by a second reviewer, with any discrepancies being resolved through agreement. RESULTS--IN VITRO CHARACTERISTICS VERSUS IN VIVO TESTING AND CLINICAL RESPONSE: There is evidence that when comparative testing is performed on inhaler devices using the same methods, there is some correlation between particle size measurements and clinical response. However, the measurements are dependent upon the methods used, and a single measure of a device in isolation is of limited value. Also, there is little data on comparing devices of different types. There is currently insufficient data to verify the ability of in vitro assessments to predict inhaler performance in vivo. RESULTS--EFFECTIVENESS OF METERED-DOSE INHALERS FOR THE DELIVERY OF CORTICOSTEROIDS IN ASTHMA: The review of three trials in children and 21 trials in adults demonstrated no evidence to suggest clinical benefits of any other inhaler device over a pMDI in corticosteroid delivery. RESULTS--EFFECTIVENESS OF METERED-DOSE INHALERS FOR THE DELIVERY OF BETA-AGONISTS IN STABLE ASTHMA: In children, 11 studies were reviewed, of which seven compared the Turbohaler with the pMDI. One study found a significant treatment difference in peak expiratory flow rate, although there were differences in the patients' baseline characteristics. In adults, a review of 70 studies found no demonstrable difference in the clinical bronchodilator effect of short-acting b2-agonists delivered by the standard pMDI compared with that produced by any other DPI, HFA-pMDI or the Autohaler device. The finding that HFA-pMDIs may reduce treatment failure and oral steroid requirement in beta-agonist delivery needs further confirmatory research in adequately randomised clinical trials. RESULTS--EFFECTIVENESS OF NEBULISERS VERSUS METERED-DOSE INHALERS FOR THE DELIVERY OF BRONCHODILATORS IN STABLE ASTHMA: In children, three included trials compared different devices with a nebuliser and demonstrated no evidence of clinical superiority of nebulisers over inhaler devices in bronchodilator delivery. A total of 23 studies in adults found no equivalence for the main pulmonary outcomes and no evidence of difference in other outcomes. RESULTS--EFFECTIVENESS OF METERED-DOSE INHALERS FOR THE DELIVERY OF BETA-AGONISTS IN COPD: Only two studies were included in this review. No evidence of clinical difference was found in beta-agonist delivery. RESULTS--EFFECTIVENESS OF NEBULISERS VERSUS METERED-DOSE INHALERS FOR THE DELIVERY OF BRONCHODILATORS IN COPD: Evidence from 14 trials demonstrated equivalence for the main outcomes of pulmonary function. For other outcomes there was no evidence of treatment difference in bronchodilator delivery. RESULTS--PATIENTS' ABILITY TO USE METERED-DOSE INHALERS: Differences among studies and the heterogeneity of the results make it difficult to draw conclusions about inhaler technique differences between device types. The review of technique after teaching the correct technique suggests that there is no difference in patients' ability to use DPI or pMDIs. RESULTS--ECONOMIC ANALYSIS: The total number of NHS prescriptions for inhaler therapy for asthma in 1998 was over 31 million, with a net

ingredient cost in excess of 392 million GB pounds. This economic assessment uses decision analysis to estimate the relative cost-effectiveness of inhaler devices for the delivery of bronchodilator and corticosteroid inhaled therapy. Overall, there were no differences in patient outcomes among the devices. On the assumption that the devices were clinically equivalent, pMDIs were the most cost-effective devices for asthma treatment. CONCLUSIONS: This systematic review examined the evidence from clinical trials evaluating the clinical effectiveness of different inhaler devices in the delivery of inhaled corticosteroids and beta2-bronchodilators for patients with asthma and COPD. The evidence from the published clinical literature demonstrates no difference in clinical effectiveness between nebulisers and alternative inhaler devices compared to standard pMDI with or without a spacer device. The cost-effectiveness evidence therefore favours pMDIs (or the cheapest inhaler device) as first-line treatment in all patients with stable asthma unless other specific reasons are identified. Patients can use pMDIs as effectively as other inhaler devices as long as the correct inhalation technique is taught. CONCLUSIONS--RECOMMENDATIONS FOR RESEARCH: Further clinical trials are required to demonstrate any differences in the clinical effectiveness and cost-effectiveness of inhaler devices and nebulisers compared with pMDIs. These should be of sufficient statistical power and methodological rigour to demonstrate any clinical benefit. Trials should be undertaken in community settings to ensure the generalisability of results. Outcome measures should be more patient-centred and report adverse effects more completely. Reporting of data from trials should be improved.

L7 ANSWER 7 OF 17 CAPLUS COPYRIGHT 2007 ACS on STN  
 TI Comparison of three treatment regimens of inhaled sodium cromoglycate in  
 the management of adult patients with severe, steroid-dependent asthma  
 AB Asthmatic patients whose asthma remains poorly controlled despite  
 treatment with high doses of inhaled corticosteroids and co-administration  
 of oral corticosteroids are a difficult problem in therapeutics. The  
 purpose of this study was to investigate the relative efficacy of three  
 treatment regimens of inhaled sodium cromoglycate in the treatment of  
 adult, severe, corticosteroid-dependent patients as determined by the  
 reduction in the dose of oral corticosteroids and change in lung function.  
 Patients whose asthma is (1) severe according to the classification of the  
 Japanese Society of Allergol., (2) stable, and (3) needing treatment with  
 at least 1600 µg of inhaled beclomethasone dipropionate and 5 mg or  
 greater of oral prednisolone per day were included in an open, randomized,  
 group comparative trial of 12 wk duration in asthmatic patients attending  
 a hospital outpatient department. The three treatment regimens of inhaled  
 sodium cromoglycate were group A received sodium cromoglycate  
 powder at a dose of 16 mg/day administered by a metered dose  
 inhaler. Group N received sodium cromoglycate aqueous soln. at a  
 dose of 80 mg/day administered by a nebulizer. Group C received sodium  
 cromoglycate aqueous soln. (80 mg/day) combined with  
 salbutamol (3 mg/day) administered by a nebulizer. The main  
 outcome measures were a change in the daily dose of oral corticosteroids  
 and in lung function with twice daily measurements of peak expiratory flow  
 (PEF) recorded in the morning (PEF AM) and in the evening (PEF PM). Mean  
 reduction in oral corticosteroid dose/day was group A, 3.68 mg (95%  
 CI 1.35, 5.95); group N, 3.59 mg (95% CI 0.73, 6.45); and group C, 3.97 mg  
 (95% CI 1.81, 6.13). The dosage redns. are all significant but with no  
 differences between the groups. The mean increase in PEF over the last 4  
 wk of treatment compared with baseline values was significant in all  
 groups. The increases in group C are significantly greater than those in  
 the other groups. These changes are all significant and the increases in  
 group C are significantly greater than those in the other groups. Inhaled  
 sodium cromoglycate may be a useful addnl. treatment in the management of  
 adult patients with severe, oral steroid-dependent asthma. Of  
 the three methods of administration compared in this trial the most useful  
 immediate results were obtained when the drug was administered as an aqueous

soln. mixed with salbutamol and delivered by a powered nebulizer.

L7 ANSWER 8 OF 17 USPATFULL on STN

TI Prilocaine and hydrofluorocarbon aerosol preparations

AB Aerosol compositions used for anesthetizing mammals in both human and veterinary applications include prilocaine base solubilized in the hydrofluorocarbon (HFC) propellants 1,1,1,2-tetrafluoroethane and 1,1,1,2,3,3,3-heptafluoropropane. Prilocaine base has been found to be readily soluble in HFC propellants when combined in liquid or micro rod form, and a solution stable to temperatures as low as -82° C. is formed upon combination of the two components. In the aerosol compositions, the HFCs are the only propellants used. Additional pharmaceutical constituents can also be combined with the prilocaine base/HFC composition to provide a multi-component anesthetic, and it has been found that the presence of prilocaine in the combination can assist in solubilizing and/or suspending these pharmaceutical constituents. Some example pharmaceutical compositions within the practice of this invention include HFC, prilocaine base, and a pharmaceutical other than prilocaine selected from the group consisting of bronchodilators, antiinflammatories, antitussives, vasoactive drugs, vasoconstrictors, antibiotics, peptides, steroids, enzymes, antihistamines, hormones, enzyme and receptor inhibitors and agonists, 5-aminolevulinic acid, antiseptics, disinfectants, procaine, cocaine, chlorprocaine, tetracaine, mepivacaine, lidocaine, bupivacaine, etidocaine, ropivacaine, benzocaine, and phenylephrine.

L7 ANSWER 9 OF 17 USPATFULL on STN

TI Method of making pressure sensitive adhesive matrix patches for transdermal drug delivery using hydrophilic salts of drugs and hydrophobic pressure sensitive adhesive dispersions.

AB A method of making a pressure sensitive matrix patch for transdermal delivery of a drug is disclosed. The method includes the steps of dissolving a hydrophilic salt form of the drug in the water phase of an aqueous dispersion of a hydrophobic pressure sensitive adhesive, casting the resulting mixture as a thin film, and evaporating the water. The physical stability of the drug in the film is excellent, and crystallization of the drug is inhibited. A method of increasing the transdermal flux of an acidic drug is also disclosed.

L7 ANSWER 10 OF 17 MEDLINE on STN

TI The delivery of aerosolized steroids from MDIs with nozzle extensions: quantitative laboratory evaluation of a method to improve aerosol delivery to intubated patients.

AB OBJECTIVE: Pulmonary deposition of aerosolized drug from a metered dose inhaler (MDI) is low with intubated patients. In the laboratory, extension of the MDI nozzle to the endotracheal tube tip has been shown to increase the delivered dose of albuterol. The objectives of this study were to determine the dose of aerosolized steroid (beclomethasone and triamcinolone) delivered through a MDI nozzle extension, the effect of nozzle extension length and number of actuations on the delivered dose, and particle size delivered through the nozzle extension. DESIGN: A 19-G catheter was used as the MDI nozzle extension. The nozzle extension was attached to a 60-ml syringe via the Luer-Lok connection, and the distal end was directed through a hole drilled into a 15-ml capped tube. The MDI was placed into the syringe and actuated by pressing the syringe plunger. Drug delivered through the nozzle extension into the tube was dissolved in methanol (beclomethasone) or ethanol (triamcinolone). Nozzle extension lengths of 10 cm, 20 cm and 30 cm were studied. For each nozzle extension length, delivery was assessed using one, two, three and five actuations of each drug. Drug remaining in the nozzle extension was recovered by rinsing with the appropriate solvent. Aerosol particle size leaving the nozzle extension was determined using a seven-stage cascade impactor.

Beclomethasone and triamcinolone concentrations were determined by spectrophotometry at 239 nm. SETTING: Respiratory care laboratory of a university teaching hospital. RESULTS: For the pooled results, 70.2 +/- 14.1% of the dose was delivered through the nozzle extension, with no difference between beclomethasone and triamcinolone ( $p = 0.838$ ). The proportion of drug delivered through the 10-cm extension (76.7 +/- 8.4%) was greater than that from the 20-cm (66.1 +/- 16.5%) and 30-cm (67.7 +/- 13.9%) extensions ( $p = 0.001$ ). Less drug was delivered through the extension with one actuation (54.1 +/- 17.7%) than with two (71.2 +/- 7.7%), three (77.2 +/- 5.5%), or five actuations (78.2 +/- 4.3%) ( $p < 0.001$ ). There was a decrease in MMAD with increasing nozzle extension length (3.14 +/- 0.61 microns for 10 cm, 2.97 +/- 0.28 microns for 20 cm, 2.37 +/- 0.27 microns for 30 cm;  $p = 0.005$ ). CONCLUSIONS: A high proportion of aerosolized steroid was delivered with a MDI actuated through a nozzle extension. The proportion delivered through the nozzle extension was significantly less with longer nozzle extensions and with fewer actuations, but this may not be clinically important. Although particle sizes were smaller from longer nozzle extensions, all were within the respirable range. These results suggest that steroids can be delivered efficiently using a MDI nozzle extension.

L7 ANSWER 11 OF 17 USPATFULL on STN

TI Phospholipid-based powders for drug delivery

AB Phospholipid based powders for drug delivery applications are disclosed. The powders comprise a polyvalent cation in an amount effective to increase the gel-to-liquid crystal transition temperature of the particle compared to particles without the polyvalent cation. The powders are hollow and porous and are preferably administered via inhalation.

L7 ANSWER 12 OF 17 USPATFULL on STN

TI Aerosol formulation containing an ester-, amide-, or mercaptoester-derived dispersing aid

AB A medicinal aerosol formulation containing a particulate drug and a dispersing aid derived from a hydroxyacid, a mercapto acid, or an amino acid.

L7 ANSWER 13 OF 17 USPATFULL on STN

TI Aerosol formulation containing an ester-, amide-, or mercaptoester-derived dispersing aid

AB A medicinal aerosol formulation containing a particulate drug and a dispersing aid derived from a hydroxyacid, a mercapto acid, or an amino acid.

L7 ANSWER 14 OF 17 USPATFULL on STN

TI Phospholipid-based powders for inhalation

AB Methods for inhalation are provided. The formulations for inhalation are engineered to be highly dispersible and provide rapid absorption of the active agent so delivered, as well as substantially independent emitted doses and lung deposition as functions of device resistance and inspiratory flow rates, respectively. The present invention also provides reductions in the flow rate dependence in lung deposition and improvements in patient reproducibility.

L7 ANSWER 15 OF 17 USPATFULL on STN

TI Pyridazinone derivatives or their salts, processes for their production, and anti-shock agents containing them

AB A pyridazinone derivative of the formula (I) or a pharmaceutically acceptable salt thereof: ##STR1## wherein Q, A, and R.sup.1 -R.sup.4 are as defined herein, useful as an anti-shock agent.

L7 ANSWER 16 OF 17 USPATFULL on STN

TI Amino acid stabilized medical aerosol formulation

AB This invention relates to a medicinal aerosol formulation and more particularly, to a medicinal aerosol formulation containing a particulate drug, a propellant and a stabilizing agent selected from an amino acid, an amino acid derivative and a mixture of the foregoing.

L7 ANSWER 17 OF 17 USPATFULL on STN

TI Prilocaine and hydrofluorocarbon aerosol preparations

AB Prilocaine base, in liquid and micro rod crystal form, can be solubilized within hydrofluorocarbon propellants to produce a stable, oily liquid. The prilocaine base can be used to solubilize additional medicaments within hydrofluorocarbon propellants that are not ordinarily soluble. The combination of prilocaine base and hydrofluorocarbon propellant can be used as an aerosolized spray to provide topical anesthesia.